EXPERIMENTAL STUDIES WITH THE DERMATOPHYTES[1]

1. Primary Disease in Laboratory Animals

EDWARD D. DE LAMATER, M.A. and RHODA W. BENHAM, Ph.D.

(Received for publication July 28, 1938)

INTRODUCTION

In the attempts to gain an insight into the pathology of infections by ringworm fungi and the associated allergy and immunity, Bloch (1) has been the primary figure. In these studies, numerous workers in addition to Bloch have used all the common laboratory animals and numerous species of dermatophytes, chiefly *Trichophyton gypseum* and *Achorion Quinckeanum*.

The course of infection in guinea pigs inoculated cutaneously by these fungi has been divided into rather clear-cut phases. These phases are: The *incubation*, 4–6 days from inoculation; the *period of spread or development* lasting 7–10 days; the *climax* which is reached by the 12th or 15th day; and, the *period of clearing* which extends from the climax to the 30th or 35th day when the skin again appears normal. Infections by *A. Quinckeanum* usually run a somewhat shorter course, clearing in 22 to 30 days.

Correlated with this picture of the disease are the histological findings of Pecori (2), Lombardo (3), and especially Hanawa (4), Saeves (5), and Martenstein (6), the latter three working primarily with *T. gypseum* infections. In guinea pigs they have observed a progressive invasion of the superficial epidermis by the fungus, accompanied by an epidermal desquamation and an inflammatory reaction in the corium which increases until the climax is reached. At this point there is a serous infiltration and an immigration of cells into the epidermis. The follicles are filled with degenerating leucocytes and there is a marked destruction of epithelium. The lesion is covered by a crust composed of detritus of nuclei, coagulated serum and horn lamellae, and an abundance of fungi. During the period of clearing, the crust separates and new epidermis forms beneath.

It has been further shown by the work of W. Jadassohn (7), and by Sulzberger (8) that in animals cutaneously infected by *A. Quinckeanum*, the fungus elements may be disseminated in the blood stream during two rather distinct periods of the disease. As Sulzberger demonstrated these periods are from 1½ to 2 hours after the inoculation (one culture was obtained on the second day) and from the 9th to 13th day after inoculation (one culture was obtained on the 6th day).

---

[1] From the Department of Dermatology, College of Physicians and Surgeons, Columbia University, New York, N. Y.

Read by title at the First Annual Meeting of the Society for Investigative Dermatology, Inc., New York City, April 30, 1938.

Infection in guinea pigs produced by other species and strains of the ringworm fungi give varying pictures from that just described. It has been noted by Bloch (1) that the more virulent the strain of fungus used, the greater the similarity of the disease produced to that of *A. Quinckeanum*. Pecori (2), Prytek (9), and Kusunoki (10) studied several strains of *T. cerebriforme*, all of which were positive on inoculation though the lesions varied in intensity. Pecori (2) working with *T. violaceum* found only two strains which were pathogenic for guinea pigs. *T. griseum* was found by Prytek (9) to produce a disease of somewhat longer course.

Of the important species of *Microsporum*, *M. felineum* has been studied by Bloch (1), Kusunoki (10), Lombardo (3), and Greenbaum (11). Lombardo found the incubation period lasting 7 to 9 days, climax about the 12th day, and cure in 50 days.

M. Audouini, a purely human form, produced a crusted inflamed area 7 to 9 days after inoculation in new-born rats, according to Bloch (1), from which he was able to get positive retrocultures. Pasini (12) was able to produce a single infection in the guinea pig and Fuhs (13) was able to produce a positive focus of lentil size in which he found one infected hair two weeks after inoculation. Such rare instances of animal infection by *M. Audouini* are believed by Bloch (1) to show that this parasite is nonpathogenic for experimental animals.

Infections with *A. Schoenleinii* as studied by Masia (14), Kusunoki (10), Thardshimanjanz (15), Seaves (5), and especially Tomasczewski (16) on a variety of animals followed an irregular course and rarely developed typical scutullae.

The disease produced by a single strain varies in different laboratory animals. Cutaneous inoculation of rabbits has been studied by Bloch and Massini (17), Lombardo (3), Tomasczewski (16), Pecori (2), and Masia (14). The course in the rabbit is less regular and usually of longer duration than that in the guinea pig. With *T. gypseum* the incubation period was from 6 to 10 days and healing took place only after 10 to 11 weeks. Reports of inoculation of other animals are relatively few.

Fungous spores were injected intravenously and intracardially at an early date by Bodin, Truffi, Citron, Sabrazès and Von Quincke (quoted by Bloch (1)), but no significant cutaneous lesions resulted. Sabrazès (18) found that the intravenous injection of *A. Schoenleinii* into rabbits and guinea pigs was often fatal but on autopsy no lesions were found except in the lungs. The former also produced pseudotubercular abscesses by intraperitoneal injection of spores. Urechia and Tataru (19) described a pseudotuberculoid granuloma following the subdural infection with *Achorion* and *Trichophyton*, and Fischer (20) described an inflammatory and destructive focus in the eye following inoculation with *Achorion*. Concerning the internal disease processes attributed to these fungi, little more is known and there are no recent confirmatory reports. Later, Sulzberger (8a), after the intracardial injection of *Achorion Quinckeanum* spores demonstrated that only skin lesions were produced although the fungi could be cultured from the inner organs with the exception of the brain, ovaries, and testes with great regularity up to the 12th day. But never were there demonstrable fungi growing in these foci *in vivo* nor was a true mycosis produced in any organ other than the skin. It was possible, however, by the sterile extirpation of the internal organs, to obtain an ample growth of fungus in them *in vitro*.

Saeves (5), Jessner and Hoffmann (21), Martenstein (6) and Kogoj (22) came to some important results by similar methods of inoculation. They demonstrated that whatever the route of internal inoculation, the site of the mycosis produced is always the skin. Only the highly sporiferous *A. Quinckeanum* and *T. gypseum* proved of value in these studies. Saeves (5) was the first to produce disseminated, crusted, infiltrated, cutaneous nodes which later developed into plaques. These lesions were grossly and histologically similar to the disease produced by superficial infection and invariably contained fungi. Spontaneous cure occurred in about three weeks. Kogoj (22) stated that the lesions produced by intracardial inoculation of *A. Quinckeanum* were regularly localized at points of skin injury.

Jessner and Hoffmann (21) reported that by the subcutaneous injection of suspension of spores in nutrient material, nodes were produced which softened and broke through the skin. From these nodes fungi could be cultured, but no new infection could be produced by inoculation with the pulp. They believed this proved that the animal body affected the pathogenicity of the fungus.

There is general agreement in all these reports that some strains of dermatophytes produce a severe cutaneous infection in the guinea pig which runs a fairly uniform course ending in spontaneous recovery. Injection of these fungi into the blood stream also produces lesions in the skin, but not in other organs. It is stated by Kogoj (22) and later thoroughly analyzed by Truffi (35) and apparently generally accepted that the occurrence and localization of these hematogenous lesions is very commonly determined by trauma. The first report of such a localization produced by trauma seems to be that of Aubert (37) 1881.

It is by no means clear whether pathogenicity for the guinea pig is a characteristic of a certain species. It seems to be the general experience that most strains isolated from human sources, if pathogenic at all, produce lesions of no such severity as those described by Bloch and his coworkers and that high virulence is exhibited by only a few strains, many of which are from sources other than the human. It is also evident from the reports noted that species other than *T. gypseum* may be pathogenic for guinea pigs and produce similar lesions. Evidently these lesions vary in their severity and course, but there is little evidence as to whether their appearance and duration are characteristic of the individual species concerned. There is divergence in opinion as to the virulence *M. Audouini*, some reporting that certain strains are mildly pathogenic for guinea pigs, others that this species is nonpathogenic.

The phenomenon of greatest interest is the cutaneous allergy so regularly developed by guinea pigs after inoculation. This will be discussed in a subsequent report. Before attempting to study the question of allergy it seemed necessary to obtain more accurate information as to the normal course of the spontaneous disease in laboratory animals and as to what variations might be encountered.

MATERIAL AND METHODS

Animals were inoculated with cultures grown on Sabouraud's honey-peptone medium for 3 to 4 weeks at room temperature. An area on the side of the abdomen and lower chest about 10 centimeters square was clipped and carefully shaved. Cutaneous inoculations were made by sandpapering the center of this area or scraping it with a scalpel and rubbing a bit of the fungus thoroughly into

the scarified area; no dressings were used. Groups of 3 to 6 animals were inoculated at the same time and in the cage with each group was placed a control animal which had been similarly shaved and scarified but not inoculated. In the case of strains 1, 2, 7 and 10, the control animal became infected from the cage mates which gave some indication of the virulence (or infectivity) of the particular strain. In this study the following strains representing the three genera of ringworm fungi were used:

	Species	*Source*
1.	*T. gypseum*	Generalized lesions of a common gray squirrel
2.	*T. gypseum*	A monkey (by Dr. C. W. Emmons)
3.	*T. gypseum*	Bullous and hyperkeratotic lesions of the feet associated with a lymphangitis of the legs
4.	*T. gypseum*	Bullous lesions of feet
5.	*T. gypseum*	Similar source (4)
6.	*T. niveum*	Finger nail
7.	*T. cerebriforme*	Non-inflammatory tinea capitis
8.	*T. violaceum*	Tinea circinata (arm)
9.	*M. felineum*	(a) Generalized tinea corporis (b) Same case
10.	*M. felineum*	Non-inflammatory tinea capitis
11.	*M. Audouini*	Non-inflammatory tinea capitis
12.	*E. floccosum*	Tinea circinata (groin)

Strain 1 was isolated from a generalized dermatophytosis of a common gray squirrel obtained in Baltimore, Md. in March, 1937. Many other infected animals were observed but only one was obtained for study. The squirrel represents a new host for the ringworm fungi. Both the causative organism and squirrel disease will be described in detail in another place (DeLamater (36)).

The clinical condition from which strain 3 was isolated has been considered in detail by Hopkins (23). The lesions consisted of a marked hyperkeratosis of the soles with large recurrent bullae. Fungi were abundant in both the thickened epidermis and in the walls of the vesicles. Fungus was also isolated from the blood of this patient. The foot lesions were accompanied by a severe lymphangitis of the legs. Both conditions had been resistant to cure for 6 years.

Strains 9a and 9b were obtained from a resistant generalized tinea corporis which has been described by Lamb (24). Both of these strains belong to the *M. felineum* species, but show, like numerous other isolates from the same source, cultural and morphological differences from one another; also, cultures proved to be very variable, showing marked tendencies to sector. Because of this, it seemed important to study more than one strain from this source.

CUTANEOUS INFECTION OF GUINEA PIGS

In order to determine the amount of variation that might be encountered in one species of animal inoculated in similar manner with the same strain of fungus, 47 guinea pigs were inoculated

cutaneously with a strain of *T. gypseum* (no. 1) which seemed unusually virulent. Observations of this series gave a standard picture by comparison with which one could determine the effect of using different strains, and of various methods of inoculation on the same animal, and similar studies on other species of animals. The lesions developed by these 47 animals showed some slight variation in the extent, the severity and the course of the infection, but on the whole they were astonishingly uniform in all these respects. Both the character of the lesions, the course and timing of their development and their involution corresponded closely to the descriptions of Bloch and other investigators whom we have quoted. The incubation period was from 4 to 6 days. Fungi were demonstrable at this time. The lesions reached a climax on the 12th to 16th day and involution was complete by the 30th to the 35th day. Attempts to demonstrate fungi were negative between the 20th and 27th day (Figs. 1–6).

The size of the lesion was probably determined by the extent of the scarification, but it is interesting that spontaneous lesions in control animals spread until they reached about the size of a 25-cent piece and then became demarcated. Scattered lesions, smaller than that in the scarified area but of similar character, often appeared on other parts of the body and about the nose, mouth and ears. They appeared to be transferred by scratching or some other form of contact.

During the period of involution, the crusts may slough off in pieces or the whole may slough out, leaving an open moist ulcer-like lesion with a raised and intensely scaling border. The scaling and inflammation gradually diminish and epilation of the diseased area occurs at this time. Following the loss of the scales, a pustular eruption in which no fungi can be found may appear on the clearing epidermis. For a few days the skin may seem thickened and leathery, but soon appears normal and the hair again begins to grow.

In all dark-skinned, or dark-eyed, light-skinned animals pigment was developed in the lesion site. Figure 7 shows such a case.

TABLE I

The course of cutaneous inoculation in guinea pigs

STRAIN	NUMBER OF GUINEA PIGS INOCULATED	INCUBATION	DEVELOPMENT	CLIMAX	CULTURE NEGATIVE	LESION HEALED	CHARACTER OF LESION
1. *T. gypseum* (squirrel).	47	4–6 days	7–10 days	12th–16th day	20–27 days	30–35 days	Marked inflammation, exudation and scaling
2. *T. gypseum* (monkey).	3	2–3 days	4–5 days	9th–10th day	15–18 days	20–23 days	Marked inflammation, exudation and scaling
3. *T. gypseum*.....	2	4–6 days	18 days	20–24 days	28–30 days	30–35 days	Marked inflammation, exudation and scaling
4. *T. gypseum*.....	6*						
5. *T. gypseum*.....	3*						
6. *T. niveum*.....	3*						
7. *T. cerebriforme*.....	2	6 days	10 days	14 days	20–30 days	35 days	Marked inflammation, exudation and scaling
8. *T. violaceum*.....	6†	12 days	5 days	None	23–24 days		Marked inflammation, but scaling only
9a. *M. felineum*.....	4	5–6 days	18–19 days	20th day	33–40 days?	45–50 days	Slight inflammation and exudation
b. *M. felineum*.....	3	5–6 days	16–19 days	20th day	25–28 days	35 days	Less inflammatory than above
10. *M. felineum*.....	6‡	4–6 days	15–16 days	21st day	43 days	50–53 days	Moderate inflammation and exudation, marked scaling
11. *M. audouini*.....	3†	14 days	6 days	20th day	28–32 days?	35 days	Slight inflammation, marked scaling
12. *E. floccosum* (groin)..	3†	4–5 days	14 days	None	23–24 days		Very slight inflammation, no exudation, superficial scaling

* None infected. † Only 1 infected. ‡ Two series.

All of the uninoculated controls used in this series became infected by their cage mates.

Several normal ginea pigs in neighboring cages and two human beings who handled the animals acquired the disease—which indicates the high infectivity of this strain (Table I).

Other strains of dermatophytes, when similarly inoculated in guinea pigs produced varying infections. Some strains elicited lesions which were indistinguishable in intensity and duration from those just considered; and some produced no manifest lesion whatever. There were many intermediate gradations, and in many cases it was difficult to observe a sharp distinction. Some strains caused small lesions with thick crusts surrounded by an inflammatory zone; others extensive lesions, which however consisted only of scaling with practically no erythema. Moreover, when two series were done at an interval of time with some of these strains, the severity and the duration of the disease differed; all of this makes the findings difficult to describe briefly. Of the strains studied, two of the *T. gypseum* strains, nos. 2 and 3, and one *T. cerebriforme*, no. 7, simulated strain 1; and three strains of the species *M. felineum*, 9a, 9b, and 10, caused lesions similar but not so severe as those produced by strain 1. In strains 3 and 7 the appearance of the lesions and the time of development and involution were practically identical; others show slight differences which may have been significant. Three animals inoculated with strain 2 ran a shorter course than those inoculated with strain 1. These differences are brought out in Table I. The crusts separated earlier and about the ulcer-like center there appeared cream-colored collars, a millimeter or more thick and several millimeters in diameter which were examined under the microscope and consisted almost entirely of mycelium and spores, thus resembling scutulla. The climax was reached in 9 to 10 days and involution was complete in 22 to 23 days.

Most of the guinea pigs inoculated with the three strains of *M. felineum* showed lesions which were less heavily crusted and showed less intense inflammation than did those inoculated with strain 1. On the other hand, a second series inoculated with strain 10 showed lesions fully as severe as those produced in any

of the *Trichophyton* animals. With strains 9a and 10 the course of the infection was somewhat more prolonged; the climax being reached by the 20th to 21st day and involution not being complete until the 45th to 53rd day. Two strains produced lesions sufficiently different in character to warrant special mention.

Microsporum Audouini. Three guinea pigs were inoculated cutaneously with *M. Audouini* and two showed no infection. The third developed a minute lesion after a prolonged incubation period of 14 days. By the 20th day this lesion had formed a heavy scab about one centimeter in diameter surrounded by a narrow zone of inflammation. The fungus was abundant in slide and was recovered in culture from these scales. The lesion healed completely in 12 to 15 days (Fig. 16).

Epidermophyton floccosum. Two guinea pigs were inoculated with strain 12. After an incubation period of four days numerous thin scales appeared over the epidermis between the hairs. The lesion increased in size and became surrounded with a very slightly inflamed border. The scales showed profuse mycelium. The hair grew back rapidly and no fungus could be found in hair removed for examination. After the 20th day the scales began to desquamate; no fungi were found on or after the 24th day and by the 35th day the area appeared quite normal. If one may judge from two animals, the disease produced by this species differed distinctly from the others observed in the lack of invasion of hairs and the slight inflammatory reaction (Table I) (Fig. 17).

The other strains used, some of which were of the same species as those which produced severe infection caused no infection whatever. The skin remained normal after the scabs formed by the trauma of inoculation had fallen away. With strain 7 a second series was inoculated several weeks after the first. A much less severe disease of shorter duration was produced, suggesting that the fungus had lost some of its pathogenicity in culture. On the other hand, with strain 10, the first series of animals showed lesions with extensive scaling but little inflammation; a later series showed an inflammatory process almost as marked as that obtained with strain 1, indicating, if anything,

that the strain had gained in virulence on being kept in culture. The virulence of the fungi for guinea pigs did not seem altogether parallel with their virulence for the human. A-virulent strains 4 and 5 were recovered from bullous eruptions on the feet which were in fact less severe than the disease in the patient from whom strain 3 was obtained; on the other hand, strain 7 which produced a very severe infection in guinea pigs was obtained from a scalp lesion which showed only a slight inflammatory reaction. There was no clear correlation between the severity of the lesions and the duration of the disease. Bloch held that in severe infections the duration was apt to be short and that in milder ones, the duration long. There was in our series some suggestion of such relationship. On the other hand, the lesions produced by strain 2 which healed in 20 to 23 days were not distinguishably more severe than the lesions produced by strains 1, 3 and 7 which healed in 35 days. One thing which seems evident from these studies is that if one is to study immunity by comparing the results of primary and secondary inoculations, it is important to use a highly virulent strain, such as strain 1 in this series, which causes infections of uniform severity and course.

Blood cultures Three groups each containing three guinea pigs were inoculated cutaneously with strain 1. Cultures were taken from the hearts of one of each group three times during the first six hours, and once daily for the next 16 days. Of these 57 blood cultures, two were positive, one taken $3\frac{1}{4}$ hours after inoculation, the other 9 days after inoculation. This agrees both as to time and rarity of the positives with the findings of Jadassohn and Sulzberger—that the fungi may occasionally be detected in the blood stream a few hours after inoculation and again during a period shortly before the climax of the disease.

Systemic inoculation (Table II). Three guinea pigs were inoculated intravenously with one cc. of a suspension of spores of strain 1 and three others similarly inoculated by cardiac puncture. The right side of the animals was then shaved and scarified as previously, but not inoculated. Three additional pigs were inoculated cutaneously as control. All six of those inoculated into the circulation developed widely disseminated cutaneous

lesions in 4 to 5 days (Fig. 8). At no time were the lesions limited to or more numerous in the previously scarified areas. These lesions which started as smaller foci enlarged to 0.5 to 2.0 centimeters and though smaller, resembled the lesions obtained by cutaneous inoculation of this strain. In two pigs inoculated intravenously, they ran a normal course and involuted as did the cutaneous lesions. The third of the intravenous group and two of the intracardial group showed a severe and prolonged course. The period of spread extended over four weeks during which time the lesions appeared all over the body and were marked on the nose and ears. They increased in size and severity until

TABLE II

Disease caused by different methods of inoculation with strain I

	CUTANEOUS SERIES	INTRACARDIAL SERIES		INTRAVENOUS SERIES	
	Normal	Abnormal—long	Abnormal—short	Normal	Abnormal
Number of animals	43	2	1	2	1
Incubation	4–5 days	5 days	4 days	4–6 days	5 days
Development	7–10 days	28 days	7 days	7–10 days	28 days
Climax	12th–16th day	Not well defined; 32nd–35th day	11th–12th day	12th–16th day	Not well defined; 32nd–35th day
Culture negative	20th–27th day	28th day	16th day	20th–27th day	56th day
Lesion healed	30th–35th day	64th day	22nd day	30th–35th day	60th day

the animals were almost entirely covered. The climax was not sharply defined and the period of involution prolonged. With the desquamation and separation of the crusts the hair fell out leaving the animals at the end of two months with a nearly hairless but otherwise normal skin. Fungi were found in the lesions for 6 weeks. In the third animal inoculated intracardially, the disease followed an abortive course. This pig was pregnant.

Disease course in pregnant guinea pigs

During the experiments already described it was noted that the disease in three animals, all pregnant females, showed interesting deviations from the normal (Table III). In two of these the disease course was completely run in 20 to 21 days. All

periods of the disease were shortened, and the climax was more acute. In each case the young were born 7 to 8 days after the lesions had cleared. In the third animal the disease was entirely normal up to the 25th day. The lesion was in the middle of the period of clearing. Very suddenly a widespread erythematous papular eruption appeared which during the following 8 to 10 days became crusted with extensively inflamed and scaly borders. These lesions cleared by cracking and sloughing with extensive epilation. The animal was finally clear 7 weeks after inoculation. The young were born on the 21st day of the disease 4 or 5 days before the relapse. To check these results 6 pregnant

TABLE III

The variable disease course in pregnant guinea pigs infected with strain I

TYPES OF COURSE	ANIMALS	INCUBATION	DEVELOPMENT	CLIMAX	CULTURE NEGATIVE	LESION HEALED
		days	*days*	*day*	*day*	*day*
Normal course....	4	4–6	7–10	12th–16th	20th–30th	30th–35th
Short course,* 21 days.....	4	4	7	11th–12th	16th	22nd
Long course, relapse†.....	1	4–6	7–10	14th	37th	45th–49th

* One inoculated intracardially.

† Two young born 21st day; relapsed by vesicular eruption 25th–26th day; 26th–36th day inflamed, exudative.

animals were inoculated with strain 1. Four gave an entirely normal course, while two gave a shortened disease similar to the two animals just described.

Course of disease in rabbits (table IV)

Four rabbits inoculated cutaneously with strain 1 showed lesions differing somewhat from those produced in guinea pigs. After an incubation period of 4 to 5 days, thin white scales appeared from which fungi could be isolated. The scaling areas extended, small crusts appeared, and about the 9th day the entire area became swollen and red. The climax was less distinct than in the guinea pigs but about the 16th to 18th day, the crusts cracked and exuded a serous fluid. New crusts formed covering

TABLE IV

The course of disease in other animals

STRAIN AND SOURCE	NUMBER OF ANIMALS	INCUBATION	DEVELOPMENT	CLIMAX	CULTURE NEGATIVE	LESION HEALED	CHARACTER OF LESION
			Cats				
1. *T. gypseum*	2 and 1 control	3–5 days	10 days	14–15 days	18th day	21–23 days	Non-inflammatory. Crust made up almost entirely of fungus elements.
9b. *M. felineum*	3, no disease 3, no disease 2 1 control caught disease	12–15 days	30th day?	None observed as clear cut	35th day 45th day	35–100 days 45–52 days	Slight exudation scaling and inflammation.
			Rabbits				
T. gypseum (squirrel)	4	4–5 days	10–12 days	16–18 days	25–26 days	32–35 days	Very inflammatory, exudative and ulcerated. Clearing in 2 phases.

the small abscesses which were apparently due to scratching. From the 19th day the inflammation and scaling diminished and by the 26th to 27th day the crusts had separated leaving a diffusely erythematous area with slight scaling. The redness and scaling finally cleared and the area became covered with new hair. Figures 9 through 12 show a sequence of stages in this disease.

PLATE I

FIG. 1. Guinea pig—Strain 1: End of incubation, 6th day. Scaling just beginning.

FIG. 2. Guinea pig—Strain 1: Period of development, 11th day.

FIG. 3. Guinea pig—Strain 1: Climax, 15th day.

FIG. 4. Guinea pig—Strain 1: Early involution, 22nd day.

FIG. 5. Guinea pig—Strain 1: Later involution, 27th day.

FIG. 6. Guinea pig—Strain 1: Late involution, 31st day. Almost clear. A few scales at border.

FIG. 7. Guinea pig—Strain 7: Clear. Hyperpigmentation produced in lesion area.

FIG. 8. Guinea pig—Strain 1: 8th day. Disseminated lesions. Animal inoculated by cardiac puncture.

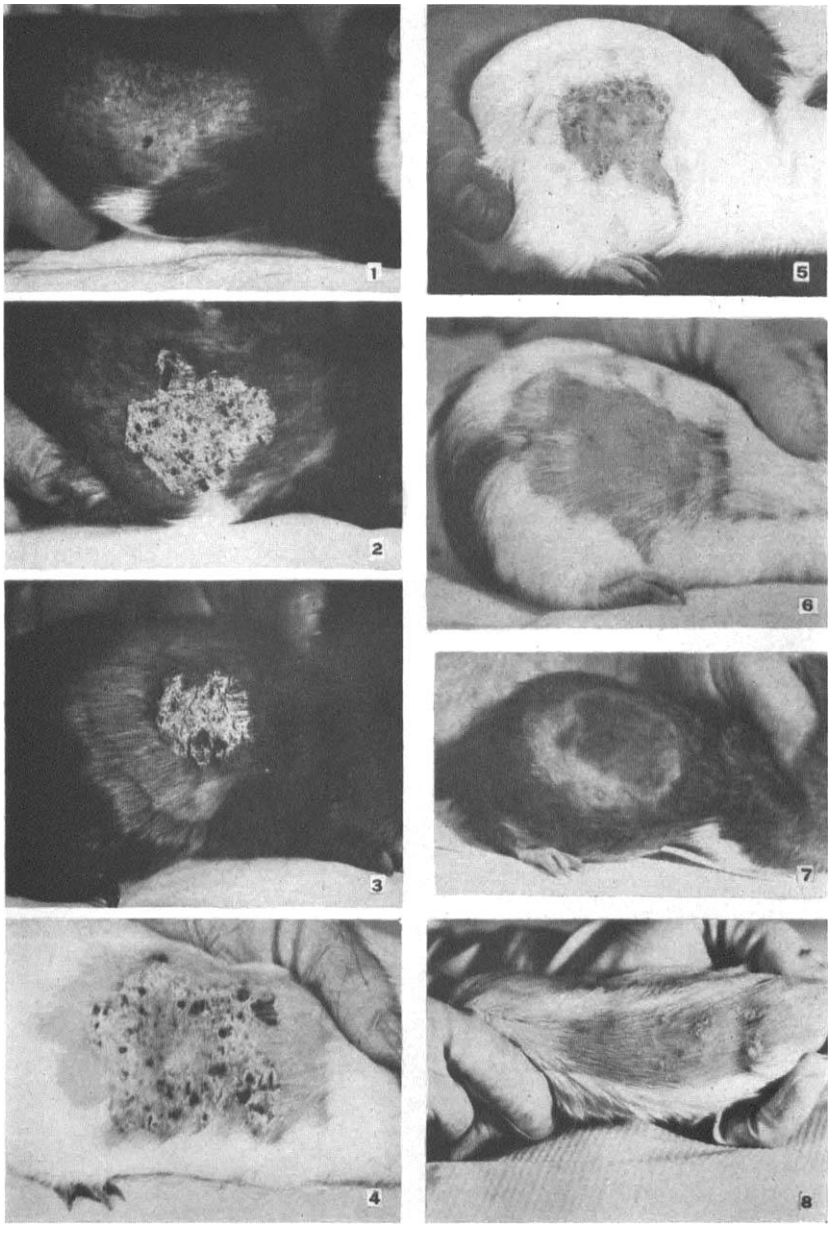

PLATE I

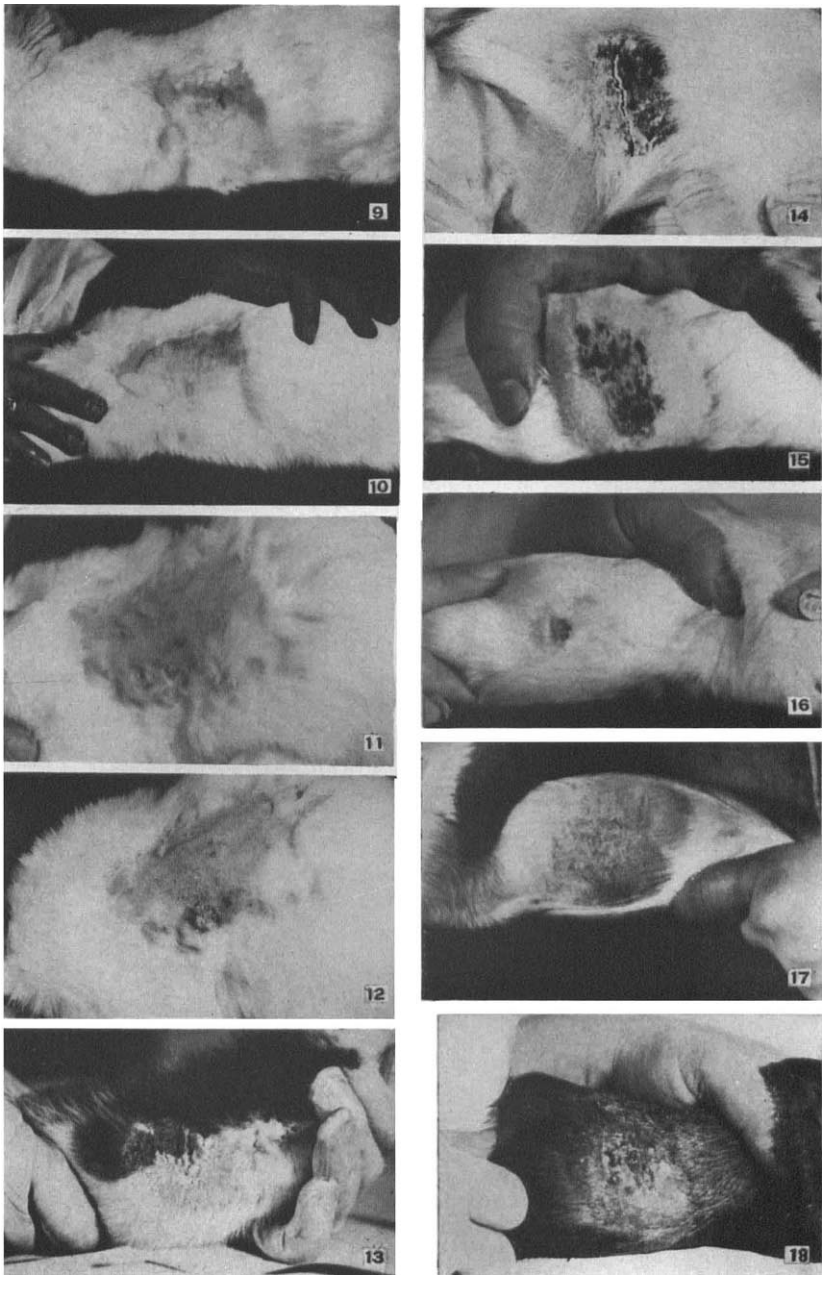

PLATE II

Ringworm infection in cats (table IV)

Three kittens inoculated cutaneously by strain 1 developed, 4 to 5 days after inoculation, scaling areas which soon became covered with dense white raised plaques composed almost entirely of fungus elements, with a few hairs. There was little inflammatory reaction and the scales fell away by the 20th to 22nd day leaving a pigmented and partly epilated but otherwise normal area of skin. Fungi were demonstrable up to the 18th day. Three series, of three kittens each, were inoculated with *M. felineum*, strain 9b. The first two series showed no evidence of infection. Animals of the third group developed crusts on the 5th day, which were distinct from those produced by scarification in the control, but which contained no fungi. These fell off about the 12th day leaving a slightly inflamed area covered with scales in which fungi could be demonstrated. Similar scaling areas continued to develop for sometime, widely scattered over the body; and on examination with Wood's Light, isolated infected hairs could be found which appeared normal on ordinary illumination. These lesions persisted for about 100 days and fungi were demonstrated as late as the 85th day. Lesions were noted on the uninoculated but scarified control cat after 44 days. They developed in a manner similar to those just described and persisted for about 2 months. These lesions were strikingly

PLATE II

FIG. 9. Rabbit—Strain 1: Early development, 9th day. Lesions indurated, inflamed and scaly.

FIG. 10. Rabbit—Strain 1: Later development, 14th day. Lesion more inflamed, indurated and scaly.

FIG. 11. Rabbit—Strain 1: Middle stage in involution, 25th day. Massive scabs still persist on lower chest.

FIG. 12. Rabbit—Strain 1: Late involution, 30th day. A few crusts still persist. Whole area covered by dense scaling.

FIG. 13. Cat—Strain 1: 15th day, showing plate of fungus material.

FIG. 14. Guinea pig—Strain 2: Climax.

FIG. 15. Guinea pig—Strain 10: Climax.

FIG. 16. Guinea pig—Strain 11: Lesions small, scaly, with narrow inflammatory border.

FIG. 17. Guinea pig—Strain 12: Diffuse, superficial scaling.

FIG. 18. Guinea pig—Strain 7: Early involution.

different from those produced by the same strain in the guinea pig and also from those produced by a strain of *T. gypseum* in cats. They suggest an adaptation of this fungus to parasitism of the cat.

Infection in man. No purposeful inoculations in humans were made in these experiments, but two persons were accidently infected in handling animals inoculated with strain 1. The incubation period could not be determined but the lesions first appeared as a group of vesicles which spread forming a central scaling area surrounded by a vesicular border. This resembled the herpetiform ringworm frequently observed in human beings, shown to be caused by either *M. felineum* or *T. gypseum.* These lesions were treated and not allowed to follow their normal course. It is important to note, however, that in human infections, spontaneous recovery which so regularly occurs in experimental animals, is rarely observed.

SUMMARY

Certain strains of dermatophytes inoculated cutaneously in guinea pigs, rabbits and cats, produced lesions of varying character and intensity.

The lesions produced by one strain of *T. gypseum* differ in these three animals, but variations also occur when different strains are inoculated in the guinea pig. The lesions vary in degree of invasiveness, amount of inflammatory reaction, in the density of the crusts formed, and in the persistence of the lesions. These variations are largely in degree and many gradations occur between a severe infection and no infection whatever.

It is notable from the work presented here, as well as from that of Prytek, Bloch, Hanawa and others, that differences which occur between strains of a single species may be as evident as those between species. Moreover, sometimes indistinguishable lesions were produced by two such distinct fungi as *T. gypseum* and *T. cerebriforme* and very similar lesions by *M. felineum.*

With one virulent strain (2) which produced a strong inflammatory reaction, the course of the disease seemed somewhat shortened. On the other hand, strains of low virulence, numbers

8 and 11 which infected only a few of the animals inoculated produced in them similar but less inflammatory lesions which also ran an abnormally short course. It would seem, therefore, that the course of the disease might be shortened either by an unusually strong reaction on the part of the host, or by the lack of virulence in the parasite. The few infections in cats with *M. felineum* which were successful caused very little inflammatory reaction but ran an extremely long course. Two strains of the same species when inoculated into guinea pigs likewise produced infections of long duration.

Injections of spores into the circulation produced widely disseminated lesions. In some animals these ran a prolonged, in others, practically a normal course. Pregnancy also seemed to cause the disease to take an abnormal course in some instances.

BIBLIOGRAPHY

The bibliography of this paper is included in that of the following.